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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,935	08/02/2001	Brigitte Bathe	211712US0X	5782
22850	7590	04/07/2006	EXAMINER	
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			HUTSON, RICHARD G	
			ART UNIT	PAPER NUMBER

1652

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/919,935

Applicant(s)

BATHE ET AL.

Examiner

Richard G. Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34,37,39-55 and 63-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34, 39-44, 46-48, 50, 51, 52, 53, 54, 55, 63-67, 69-73 and 81 is/are rejected.
- 7) ☒ Claim(s) 37,45,49,68 and 74-80 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 1/23/2006 has been entered.

Applicants cancellation of claims 36, 38, 56-62 the amendment of claims 34, 39, 54, 70-73, in the paper of 1/23/2006, is acknowledged. Claims 34, 37, 39-55, 63-81 are still at issue and are present for examination.

Applicants' arguments filed on 1/23/2004, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 37, 45, 49, 68, 69 and 73-80 are objected to because of the following informalities:

Claims 37, 45, 49, 68 and 73-80 are dependent on rejected claim 34.

Claim 69 is objected to because it reads poorly, such that it is unclear. It is suggested that the proper usage of commas to within the claim could alleviate such confusion.

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Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52 and 69-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 52 and 69-72 are directed to all possible methods of expressing the polynucleotide of claim 34 comprising conditions which prolong the life of mRNA or prevent the degradation of methylene tetrahydrofolate reductase (claim 52) or involve the reduction or enhancement of additional polynucleotides involved in an amino acid metabolic pathway (claims 69-72). The specification, does not describe any methods, means or mechanisms of alteration of protein or polynucleotide expression encompassed by these claims. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

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Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 52 and 69-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide which encodes a protein having the amino acid sequence of SEQ ID NO: 2, wherein said protein has methylene tetrahydrofolate reductase activity, does not reasonably provide enablement for any method of expressing said polynucleotide which further comprises the reduction or enhancement of additional polynucleotides involved in an amino acid metabolic pathways. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 52 and 69-72 are so broad as to encompass any method of expressing said polynucleotide of claim 34, which further comprises the

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reduction or enhancement of any polynucleotides involved in an any amino acid metabolic pathways. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large polynucleotide sequences and means of enhancing and/or reducing their expression encompassed by the claims. However, in this case the disclosure is limited to those methods of expressing the nucleic acid of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions, modifications, or phenotypes as encompassed by the instant claims. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all methods of modifications of expression of any polynucleotide involved in any amino acid metabolic pathway because the specification does not establish: (A) those polynucleotides and their controlling regions which may be modified effecting their activity; (B) the general tolerance of the metabolic pathway polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying the expression of said polynucleotides with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to result in the desired

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modification of expression, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of expressing the polynucleotide of claim 34, which further comprises the reduction or enhancement of additional polynucleotides involved in any amino acid metabolic pathway.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method of expressing the polynucleotide of claim 34, which further comprises the reduction or enhancement of additional polynucleotides involved in any amino acid metabolic pathway. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of methods or means having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,

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except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following rejection is based on the newly discovered reference(s) of Pompejus et al. (US Patent Application Publication 2005/0260707 A1).

Rejection(s) based on the newly cited reference(s) follow(s). The reference has not been applied previously as it was published only after the mailing of the prior Office action. The examiner regrets any inconvenience this may cause applicant.

Claim(s) 34, 39-44, 46-48, 50, 51, 53, 54, 55, 63-67, 71, 73 and 81 are rejected under 35 U.S.C. 102(e) as being anticipated by Pompejus et al. The claims are drawn to a nucleic acid comprising SEQ ID NO:1, or a fragment of SEQ ID NO: 1, which encodes a polypeptide having methylene tetrahydrofolate reductase activity, a vector, a host cell and methods of expression of a host cell comprising said nucleic acid.

Pompejus et al. teaches a nucleic acid, SEQ ID NO:673, that is 99.6% identical to nucleotides 364 to 13685 of SEQ ID NO:1 herein (see Appendix A), a complement thereof, a vector comprising said nucleic acid, and a host cell, including a bacterial host cell, comprising said vector and method of expressing and isolating amino acids from host cells expressing said nucleic acid.

This anticipates claims 1, 5-7, 18-29, and 33 as written.

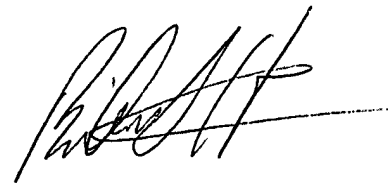
SEQ ID NO:673 of Pompejus et al. was first disclosed as RXA02717 in provisional application 60/141,031, filed on 6/25/1999.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rg
3/30/2006